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10/516,587	06/24/2005	Akiko Nishi	12218/42	5532

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EXAMINER	
WALICKA, MALGORZATA A	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/516,587	NISHI ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,7,9-12,15,17-20 and 23-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4,12,17 and 20* is/are allowed.

6)☒ Claim(s) *3,7,9-11,15,18,19,23-30 and 33-39* is/are rejected.

7)☒ Claim(s) *31 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/09/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The Amendment of May 8, 2006 is acknowledged. Claims 1, 2, 5, 6, 8, 13, 14, 16, 21 and 22 have been cancelled. Claims 3, 4, 7, 10, 1-12, 15, 17, 19, 20, 23 –26, 30, 34-36 and 39 have been amended. Claims 3, 4, 7, 9-12, 15, 17-20 and 23-39 are pending and under examination.

DETAILED ACTION

1. Priority

Acknowledgment is made of applicants' claim for priority based on an application number 2002-165722 filed in Japan on 06/06/2002. Applicants filed the priority document, however it is not translated. SEQ ID NO: 1 and 2 are disclosed in the priority document, as well as are drawings presenting data for wild type acylase set forth by SEQ ID NO: 2. The Japanese application does not seem to disclose mutated SEQ ID NO: 2 and effects of mutation, which are only shown in PCT/JP03/06807. In result claims 4, 5, 6, 7, 11-19, 21, 22, 25-38 are entitled only to the priority date of filing of the PCT/JP03/06807 application, which is May 30, 2003.

2. Objections

2.1. Specification

The objection to the specification has been withdrawn, because the amendment was entered.

2.2. Claims

The objections to claims 8-9, 11, 12, 13, 14, 15, 16 and 17 made in the Office action of Feb. 7, 2006 (previous action) are withdrawn because the claims have been corrected.

Objections caused by amendment

Claim 3, 15 is objected to for the recitation "enzymatically deleted after translation and having beta-lactam acylase activity". Firstly, the signal sequence is cleaved off, and secondly it can be cleaved off only after translation because there is no protein before translation. Thirdly, a polypeptide having a certain enzymatic activity does not lose it after its signal sequence is cleaved off in the process of protein maturation. The signal sequence is not related to the enzymatic activity.

In claims 31-32 please only use the names of cell lines, which are given in parenthesis and please omit the parenthesis.

3. Rejections

3.1. 35 USC section 101

Claim 1-9, 11-27, 29-30 and 34 were rejected under 35 U.S.C. 101 in the Office action of Feb. 7, 2006 (previous action). Rejection of claims 1-2, 5-6, 8, 13-14, 16, 21 and 22 is moot because the claims have been canceled. Rejection of claims 3-4, 7, 9-12, 15, 17-20, 23-30 and 34 is withdrawn because the claims have been amended.

Claim 28 is rejected because it still reads on a whole organism, including human bing, because, as suggested by the language of the claim a transformant is obtainble by

transforming a host cell. The scope of the claim suggested by its language encompasses a whole organism that is obtained out of a transformed cell.

3.1. 35 USC, section 112, second paragraph

Claim 4-8, 14-16, 18-38 were rejected under 35 U.S.C. 112, second paragraph, in the previous action. Rejection of claims 5, 8, 14, 16 and 21-22 is moot because the claims have been cancelled.

Claim 4, 7, 12 and 15 were rejected in the previous action as confusing because they do not state that the claimed gene encodes a protein comprising SEQ ID NO: 2, wherein this sequence was modified at residue 204, or at plurality of amino acid residues. This rejection is now withdrawn, because the claims have been amended.

Rejection of claim 9 as being multiple depended is withdrawn.

Claims 20 and 23 were ejected in previous action as confusing, because the calims did not state that the claimed protein comprises SEQ ID NO: 2, which was modified at residue 204, or at plurality of amino acid residues. This rejection is now withdrawn, because the claims have been amended.

Rejection of claim 26 is withdrawn, because the claim has been amended.

Claims 27 and 34-38 was rejected as multiply dependent. This rejection is now withdrawn, because claims 1-2 has been cancelled, and claim 3 has been amended.

Furthermore, claim 35 was rejected as directed to an immobilized cell disrupted product. This rejection is withdrawn because the claim has been amended.

Rejection caused by amendment or maintained

Claims 3, 11, 19 and 23 recite the phrase "not less than 90% in total" which is not clear. For examination purposes it is assumed that the homology is at least 90%. Dependent claims 9, 24, 25-30, 33, 34, 37 and 38 are included in this rejection because they do not correct the language of the base claim from which they depend.

Claims 28, 36 and 39 are rejected because

1) it is confusing as to whether the transformant is the whole organism initiated from a transformed cell, as suggested by the language "obtainable" and
2) it is not clear whether a host cell is transformed in the organism containing the host cell or it is an isolated host cell. Applicants do not disclose a transformed organism.

Claim 39 is rejected as confusing. For examination purposes it is assumed that Applicants intend to claim an immobilized beta-lactam acylase which is obtained by culturing an isolated cell transformed according to claim 28.

2.2. 35 USC, section 112, first paragraph

2.1.1. Lack of written description

Withdrawals/cancellations

Rejection of claims 1, 5, 6, 13, 14, 15, 21, and 22 is moot because the claims have been cancelled.

Rejection of claims 31 and 32 is withdrawn because the attorney of record provided a statement over his/her signature and registration number, stating that the

specific strain has been deposited under the Budapest Treaty and that the strains will be available to the public under the conditions specified in 37 CFR 1.808; see the current amendment in REMARK, page 8.

Rejection of claims 19-20 is now withdrawn because the function of the variants has been explicitly stated.

Rejection of claims 9, 10 and 18 is now withdrawn, because claim 3 and 11, from which claims 9, 10 and 18 depend, have been amended.

Rejection of claims 24-25 for lack of structure of transcription and translation regulatory sequences is withdrawn, because the claims have been amended.

Rejection of claim 35 for lack of written description of how to immobilize any cell disrupt product from any Stenotrophomonas so that it contains an immobilized beta-lactam acylase is withdrawn, because the claim has been amended.

Rejection maintained or caused by amendment

Claim 10 is rejected because the invention appears to employ novel strain Stenotrophomonas maltophilia KNK12A strain. Since the strain is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The enablement requirements of 35 U.S.C. section 112 may be satisfied by a deposit of the strain. The specification does not disclose a repeatable process to obtain the Stenotrophomonas maltophilia KNK12A strain and it is not apparent if this strain is readily available to the public. Accordingly, it is deemed that a deposit of the strain should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein.

The claims 7, 15 and 23 remain rejected because neither the specification nor claims disclose a signal sequence at the N-terminal site of SEQ ID NO:2. The specification does not teach that protein of SEQ ID NO: 2 is a subject of any posttranslational cleavage off. On page 12 of the specification Applicants exemplifies in general terms the meaning of the term "modification after translation" as referring to an enzymatic cleavage off of the 20 N-terminal amino acids which serve as signal sequence required for a move of protein to a periplasm region of a microorganism. However, Applicants do not teach any N-terminal region of SEQ ID NO: 2 that is not necessary for its catalytic activity and is cleaved off posttranslationally. The signal sequence of SEQ ID NO: 2 must not consist of 20 amino acids, because it may be longer or shorter.

For the above explained reasons Applicants have failed to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention when the application was filed.

2.2.2. Scope of enablement

Claim 1, 3, 5, 6, 7, 9, 10, 13, 14, 15, 18, 19, 21, 22, 23, 24, 25, 27-30, 33-39 were rejected in the previous action for scope of enablement.

Cancellations and withdrawals

Rejection of claims 1, 5, 6, 13, 14, 21 and 22 is moot because the claims have been cancelled.

Rejection of claim 10, 24, 25 and 35 is withdrawn, because the claims have been amended.

Claims 3, 7, 9, 11, 18, 19, 24, 25, 27, 29, 30, 33, 34, 36, 37 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a) a DNA molecule of SEQ ID NO: 1 encoding beta-lactam acylase from Stenotrophomonas maltophilia KNK12A,

b) beta-lactam acylase of SEQ ID NO: 2 from Stenotrophomonas maltophilia KNK12A, and its immobilized form,

(c) Met204Val mutant of beta-lactam acylase of SEQ ID NO: 2 from Stenotrophomonas maltophilia KNK12A,

(d) a microorganism or isolated cell transformed with a)

(e) a method of producing a beta-lactam antibiotic by using beta-lactam acylase of SEQ ID NO: 2 or its improved mutant Met304Val,

does not reasonably provide enablement for

(A) a beta lactam acylase that is 90% identical to SEQ ID NO:2 and its use for production of antibiotics, and

(B) a DNA molecule coding for (A), and

(C) any transformant including a whole organism transformed with a), and

(D) a method of use A) for antibiotics production.

The scope of the claims covers a large and variable genus of DNA molecules, and proteins, mentioned at (B) and (A) and for that matter expression vector and transformed cells, as well as methods of recombinant production of said proteins, as well as processes of using of said proteins for production of beta-lactam antibiotics, wherein the guidance for structure of polynucleotides and proteins mentioned at (B) and (A) is clearly lacking.

While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the claimed species have the functionality of beta-lactam acylase. The provision of SEQ ID NO: 1 and 2 and the mutant substituted in amino acid residue 204 of SEQ ID NO: 2 fails to provide such guidance of polynucleotides and polypeptides with structural variations therefrom which remain encompassed within the scope of the rejected claims. The polynucleotides and polypeptides are from any natural source, man-made or from any species of the genus of Stenotrophomonas. Applicants attention is turned to the fact that a sequence that is 90% SEQ ID NO: 2 is not enabled absent teaching how to modify SEQ ID NO: 2 so that it still possesses the required activity of beta-lactam acylase. Providing mutation in position 204 is not instructive for the claimed major structural changes that are neutral for the activity of beta-lactam acylase.

In conclusion, one of skills in the art would require more guidance than provided

in the instant disclosure, in order to make and use the invention which reasonably commensurates with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

In addition, claims 28, 36 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for which is a microorganism or for any isolated host cells which is transformed with the claimed gene or polynucleotides, does not reasonably provide enablement for all possible host organisms similarly transformed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons explained in details in previous action. Therefore, one of ordinary skill would require guidance, in order to make and use host organisms in a manner reasonably commensurate with the scope of the claim. Without such guidance, the experimentation left to those skilled in the art is undue.

In addition, claims 7, 15 and 23 remain rejected because neither the specification nor claims disclose a signal sequence at the N-terminal site of SEQ ID NO:2. The specification does not teach that protein of SEQ ID NO: 2 is a subject of any posttranslational cleavage off. The specification is silent as to any N-terminal region of SEQ ID NO: 2 that is not necessary for its catalytic activity and is cleaved off posttranslationally. Providing SEQ ID NO:2 is not a sufficient guidance for cleavage of its N-terminal signal sequence when such sequence is not identified by Applicants. Those skilled in the art realize that signal sequences are of different length. Thus one having skills in the art is left with experimentation that is unnecessary and undue.

2.3. 35 USC section 102

Claim 6, 14, 22, 26, 27, 29 and 34 were rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,168,048, issued Dec. 1, 1992, included in the Information Disclosure Statement.

Withdrawals/cancellations

Rejection of claims 6, 14 and 22 is moot because the claims have been canceled. Rejection of claims, 26, 27, 29 and 34 is withdrawn, because the claims have been amended.

3. Conclusion

Claims 4, 12, 17 and 20 are allowed for reasons stated in the previous action. Claims 31 and 32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 3, 7, 9, 10, 11, 15, 18, 19, 23-30, and 33-39 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1652

Patent Examiner

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